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(56) Documents Cited

WO 97/38955 A

(58) Field of Search

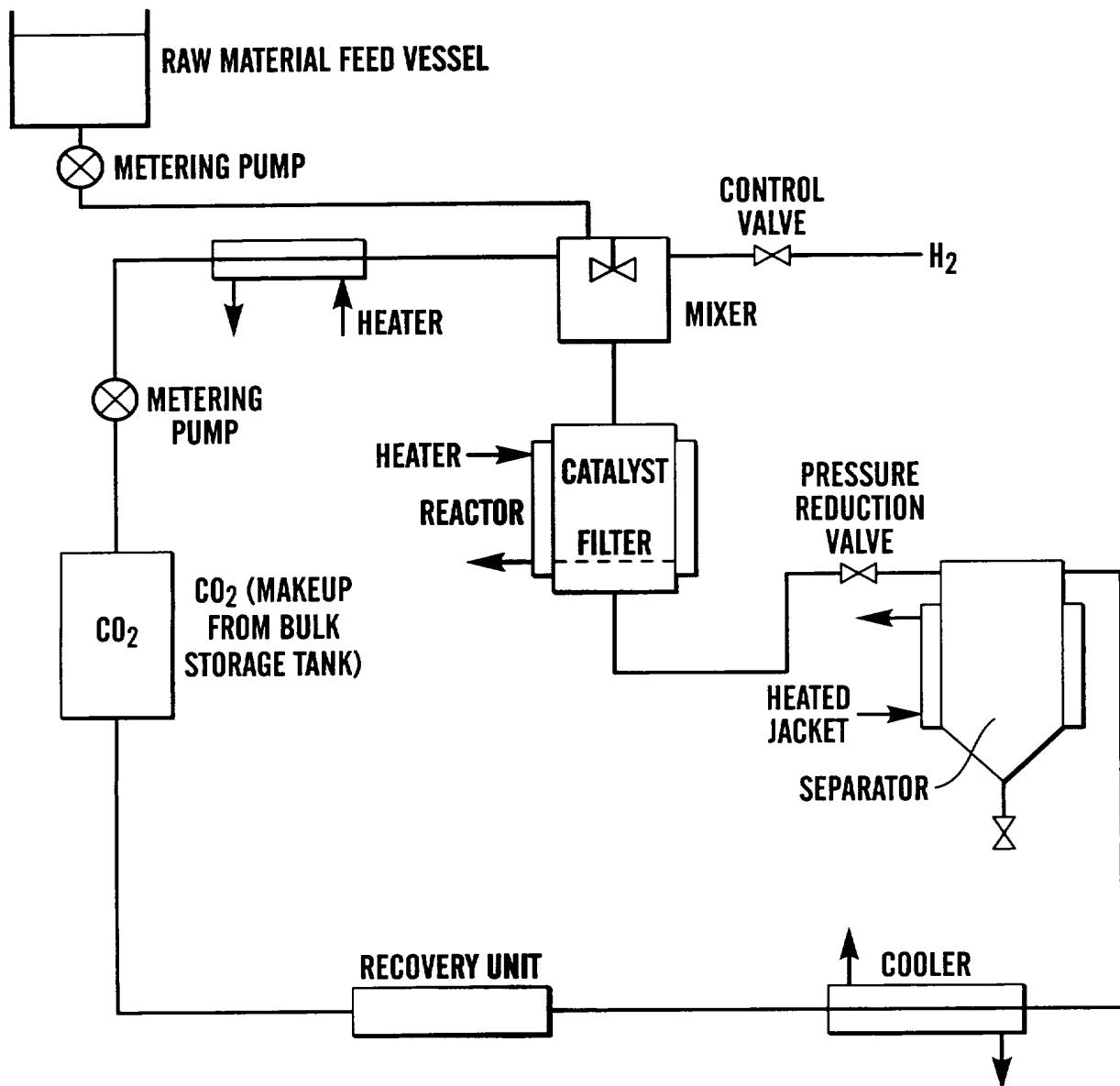
UK CL (Edition P) **C2C CAH CUF**
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(54) Abstract Title

HYDROGENATION OF HOP ACIDS

(57) Hop acids are hydrogenated by mixing hydrogen and a solution of hop acids in super-critical carbon dioxide and bringing the mixture into contact with a noble metal catalyst. Typically, the hydrogenation is used to convert iso- α -acids to tetrahydroiso- α -acids, for which palladium is especially suitable as catalyst.

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SUPERCRITICAL CARBON DIOXIDE
HYDROGENATION PLANT

HYDROGENATION OF HOP ACIDS

This invention is concerned with the hydrogenation of hop acids, and in particular the hydrogenation of iso- α -acids (isohumulones) to tetrahydro-iso- α -acids (tetrahydroisohumulones).

Tetrahydroiso- α -acids are established in the brewing industry as potent bittering and foam-stabilizing agents. They are conveniently manufactured by catalytic hydrogenation of aqueous and alcohol solutions of iso- α -acids (Brown *et al*, 10 Chemistry of Hop Constituents, Part XII, J. Chem. Soc (1959) p. 545-551). Iso- α -acids are obtainable by heat treatment of α -acids, carrying out the isomerisation *in situ* in pelletised hops (see for example GB-A-2,213,163) or after extraction from hops.

Hop acids may be extracted from hops using liquid carbon dioxide or super-critical carbon dioxide (see for example GB-A-2,119,399). Also it has been proposed to hydrogenate functional groups in organic compounds by carrying out the reaction in super-critical fluids (see for example WO 97/38955).

The present invention aims to overcome problems associated with conventional manufacturing production of tetrahydro-isohumulones: such as low yield; production of a product with tendency to precipitate out during ambient storage; the need to use flammable solvents, or if flammable solvents are not being used, the need to carry out the process at high dilution; and high catalyst cost due to fouling of the catalyst by hot resin components.

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This invention is based on the discovery that hop acids are soluble in super-critical carbon dioxide and that the unsubstituted side chains of hop acids can be hydrogenated effectively and without hydrogenolysis of the acids by carrying out the hydrogenation in super-critical carbon dioxide; also that tetrahydro product can be obtained at high yield, with only negligible amounts of dihydro and hexahydro products.

Accordingly, the present invention provides a process for hydrogenating hop acids

comprising forming a solution of hop acids and hydrogen in super-critical carbon dioxide and contacting the solution with a noble metal catalyst.

Typically, the hydrogenation is used to convert iso- α -acids to tetrahydro-iso- α -acids. 5 However, the same procedure may be used to hydrogenate the unsaturated side chains of other hop acids such as alpha-acids (humulones) and rho-iso- α -acids. Rho-iso- α -acids are a useful starting material for the preparation of hexahydro-iso- α -acids. The process of this invention is especially suitable for substantially 100% conversion of iso- α -acids to tetrahydro-iso- α -acids. However, by adjustment of the relative amounts 10 of starting material and hydrogen, catalyst content and catalyst contact time, production of dihydro-acids or mixtures of acids of different degrees of hydrogenation may be obtained. Depending on the brewers requirements for bitterness and foaming properties, in some situations a blend of dihydro and tetrahydro-iso- α -acids is desirable. It will be appreciated that natural hop acids are a mixture of homologues 15 with varying acyl side chains, such as iso-butyl, iso-propyl and sec-butyl, and so as is customary in this field references to α -acids etc. include all the relevant homologues.

Noble metal catalysts conventionally used for hydrogenation of hop acids may be used 20 in the present process. Palladium is especially suitable for the preparation of tetrahydro-iso- α -acids, and is typically used as from 5% - 10% palladium supported on carbon or alumina. Platinum is also suitable.

The hydrogenation may be carried out as a batch process or as a continuous flow 25 system, the latter being preferable for commercial scale production.

To ensure the carbon dioxide is in the super-critical state, the process is operated at a pressure greater than 73 bar and a temperature above 31°C. Normally, the pressure will not exceed 1000 bar, and is typically in the range of 200 to 350 bar. The 30 temperature is suitably in the range of 35 to 100°C. Preferably the temperature is above 40°C and typically around 75°C.

In the above pressure range it has been found effective to add hydrogen to a partial pressure of 20 bar when preparing tetrahydro hop acids.

The hop acids are typically present in solution at a loading of about 2.5 - 5% wt/vol.

5 To increase the loading of hop acids, it may be necessary to increase the pressure of the system to ensure full solution.

The product may be recovered by depressurising a batch system or in a continuous flow system bringing the solution sub-critical and evaporating carbon dioxide for

10 recirculation.

The process of this invention is illustrated by the following Examples.

In the Examples, hydrogenation experiments were carried out using a 182 ml
15 autoclave equipped with sight glass windows and a stirrer. Pure isohumulones and catalyst were loaded into the autoclave in quantities mentioned below. The autoclave was pre-pressureized to 20 bar with hydrogen gas and then pressureized to about 205 bar with carbon dioxide gas. To assess the progress of the reaction samples were taken at regular intervals via a valved sampling port, dissolved in ethanol, and
20 analysed using HPLC. Occasionally it was necessary to reintroduce carbon dioxide to maintain pressure due to pressure loss as a result of sample removal, and as a result the pressure varied between 200 and 220 bar during the tests.

Example A

25 The autoclave was loaded with 5g of isohumulone and 0.5g of a catalyst consisting of 10% palladium on carbon. The reaction was allowed to proceed at a temperature of about 40°C with the stirrer being switched on after 24 minutes. After 100 minutes, analysis revealed that 100% conversion of isohumulone to tetrahydro-isohumulone had taken place.

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Example B

Example A was repeated but with the amount of isohumulones increased to 10g. The

stirrer was switched on after 35 minutes. After 160 minutes the reaction mixture consisted of approximately 80% tetrahydro-isohumulone, 10% dihydro-isohumulone and 10% isohumulone.

5 **Example C**

Example B was repeated with the temperature increased to 75°C, starting the stirrer at 35 minutes. After 80 minutes 100% conversion of isohumulone to tetrahydro-isohumulone was achieved. Unlike the previous two Examples, the monitoring of the reaction showed that very little dihydro-isohumulone was produced in the course of
10 the reaction.

In the above Examples, a laboratory scale batch process was used to establish the efficiency of the process. In commercial production of hydrogenated hop acids, a continuous flow system is preferred. The single Figure of the accompanying drawings
15 shows, by way of example only, a schematic drawing of a continuous flow system for hydrogenation of hop acids.

In the process illustrated hop acids (typically isohumulones) are fed from a raw material feed vessel to a mixer which is also fed with hydrogen and carbon dioxide under pressure and temperature conditions which result in the carbon dioxide being
20 in a super-critical condition. The temperature of the mixture is controlled by the temperature of the main constituent of the mixture, the carbon dioxide, which passes through a heater on route to the mixer. From the mixer the reaction mixture is fed to a reactor containing a bed of the selected catalyst. The reactor is also provided with a heater jacket to control the reaction conditions. From the reactor the mixture containing hydrogenated product passes through a pressure reduction valve into a separator, where under sub-critical conditions carbon dioxide is evaporated from the reaction mixture. This allows the hydrogenated product to be recovered from the separator, while evaporated carbon dioxide is fed via a cooler to a recovery unit for
25 recirculation back to the mixer, to continue the reaction cycle with fresh input of reactants.
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CLAIMS

1. A process for hydrogenation of hop acids comprising forming a solution of hop acids and hydrogen in super-critical carbon dioxide, and contacting the solution with 5 a noble metal catalyst.
2. A process according to claim 1 in which a continuous flow of the solution is passed through or over a bed of the catalyst.
- 10 3. A process according to claims 1 or 2 in which the hydrogenation is carried out at 73-1000 bar.
4. A process according to claim 3 in which the hydrogenation is carried out at 200 - 350 bar.
- 15 5. A process according to any one of claims 1 to 4 in which the hydrogenation is carried out at a temperature of 35-100°C.
6. A process according to any one of claims 1 to 5 in which iso- α -acids are 20 converted to dihydroiso- α -acids or tetrahydroiso- α -acids or a mixture thereof.
7. A process according to any one of claims 1 to 5 in which α -acids are converted to tetrahydro- α -acids or dihydro- α -acids or a mixture thereof.
- 25 8. A process according to any one of claims 1 to 5 in which rho-iso- α -acids are converted to hexahydroiso- α -acids.

Amendments to the claims have been filed as follows

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CLAIMS

1. A process for hydrogenation of hop acids comprising forming a mixture of hop acids, hydrogen and carbon dioxide, bringing the mixture to a pressure greater than 73 bar and a temperature above 31°C so that the carbon dioxide is in a super-critical state, and bringing the mixture into contact with a noble metal catalyst.
2. A process according to claim 1 in which a continuous flow of the solution is passed through or over a bed of the catalyst.
- 10 3. A process according to claims 1 or 2 in which the hydrogenation is carried out at 73-1000 bar.
4. A process according to claim 3 in which the hydrogenation is carried out at 15 200 - 350 bar.
5. A process according to any one of claims 1 to 4 in which the hydrogenation is carried out at a temperature of 35-100°C.
- 20 6. A process according to any one of claims 1 to 5 in which iso- α -acids are converted to dihydroiso- α -acids or tetrahydroiso- α -acids or a mixture thereof.
7. A process according to any one of claims 1 to 5 in which α -acids are converted to tetrahydro- α -acids or dihydro- α -acids or a mixture thereof.
- 25 8. A process according to any one of claims 1 to 5 in which rho-iso- α -acids are converted to hexahydroiso- α -acids.



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Claims searched: 1-8

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Patents Act 1977
Search Report under Section 17

Databases searched:

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

UK Cl (Ed.Q): C2C(CUF, CAH)

Int Cl (Ed.6): C07C-45/62 ; C07C-49/743

Other: DATA-BASE: CAS-ON-LINE

Documents considered to be relevant:

Category	Identity of document and relevant passage	Relevant to claims
X	WO 97/38955 THOMAS SWAN & CO., LTD	ALL

X Document indicating lack of novelty or inventive step
Y Document indicating lack of inventive step if combined with one or more other documents of same category.
& Member of the same patent family

A Document indicating technological background and/or state of the art.
P Document published on or after the declared priority date but before the filing date of this invention.
E Patent document published on or after, but with priority date earlier than, the filing date of this application.